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The Relationship between Fatty Acids and Infertility Resulting from Obesity in Women

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Abstract
Obesity is considered one of the more prevalent diseases of our time, especially among women, and it greatly affects many metabolic pathways, especially fat metabolism, and is considered a risk factor for many other diseases. Many studies have demonstrated the role of obesity as one of the contributary factors in female infertility. The current study considered two groups of obese women with infertility ranging between 5-30 years and women with normal weight and without infertility. The results of the current study showed significant differences in the levels of various fatty acids, common and unsaturated, between the two groups of infertile and fertile women. This is indicative of the role of obesity in fatty acid metabolism and for it being considered one of the main contributary factors in infertility. It is also possible to consider the results for the fatty acids as an indicator of the occurrence of cases of infertility among obese women.
Keywords: *infertility, obesity, fatty acids.*

INTRODUCTION

The failure to conceive after one year of marriage in women under the age of 35 (and six months in women over the age of 35) is medically known as infertility, and which is a disease that can affect both the female and male reproductive systems. [1] A study conducted in 2020 showed that infertility among females is 33-40%, and in males is 25-39%, with the following areas being most affected, constituting 30% of the world's regions: Eastern Europe, Central and Southern Asia, and the southern region of the Sahara [2] [3]. There are two types of infertility: primary infertility, which is the failure to become pregnant at all, despite the absence of any obstacle; and secondary infertility, which is the failure to become pregnant after a previous pregnancy, whether the previous pregnancy ended in a live birth, a stillbirth, or a miscarriage. According to a recent study conducted by the World Health Organization (WHO), infertility was found to be a global problem, and has accordingly caught the interest of various research groups [4]. Infertility is a risk that threatens the dreams of many couples worldwide of achieving parenthood, regardless of location. The most important of these causes may be genetic (mutations), chromosomal abnormalities, and lifestyle factors (such as unhealthy eating habits and smoking), and which have also attracted research interest (as obesity has the potential to negatively affect female organ functions in the long term) [5]. The causes of infertility may be known or unknown, and whether they are related to women or men, and they may be medical, biological, or psychological (psychological) [6] [7], including such issues as anxiety, stress and depression, ovulation dysfunction, and polycystic ovary syndrome (PCOS). A common factor in infertility is obesity because this is linked to lifestyle, as a high-calorie diet changes the energy status, which affects the body's metabolic processes. Also, in contrast to obesity, weight loss resulting from malnutrition and strenuous exercise also affects female fertility. These factors lead to changes in the hormonal profile, which have a concomitant effect on the insulin and fat metabolism pathways, and which have been shown to play an important role in reproductive health [5] [9]. Due to the increasing prevalence of obesity, the WHO considers obesity to be an epidemic that affects the reproductive capacity of both sexes. For example, in males, it affects sperm in terms of their shape, movement, and viability. Obesity can increase the incidence of gynecological diseases such as endometriosis, uterine fibroids, polycystic ovary syndrome, preeclampsia, miscarriage and infertility due to the amount of fat stored in the abdominal area, in particular. In women, reproductive capacity is negatively affected due to changes in the hypothalamus-pituitary-ovarian axis. Insulin levels in the bloodstream are often high in obese women, which in turn affects androgen levels, which increase through their formation by the ovaries and converts them to estrogen. This has a negative effect on the hypothalamus-pituitary-ovarian axis. These hormonal changes result in disruption of the menstrual cycle and ovulation. This may further worsen to polycystic ovary syndrome, which promotes the deposition of visceral fat due to hyperinsulinemia, thus preventing pregnancy [11]. In a study conducted on obese women in Iraq in 2023, obesity was linked to decreased fertility because it can disrupt hormonal balance and weaken ovulation. Women with extreme obesity may experience an increase in the hormone LH due to an increase in the hormone estrogen, which works to provide more than one egg from each ovary repeatedly, leading to a disruption in the menstrual cycle and the failure to become pregnant. High estrogen also works to inhibit the hormone FSH, which may prevent ovulation. In general, obesity has a negative effect on LH and FSH levels, which means problems with pregnancy and decreased ovulation and fertility in women who suffer from obesity [3]. In Denmark, for example, delayed pregnancy was observed, as was weak fertility despite the natural ovulation process. Another study was conducted on 3,000 Dutch women with a body mass index of more than 30 kg/m^2 and who had regular menstrual cycles yet who had failed to become pregnant. This was repeated in the United States, where the same conclusion was drawn, namely that obesity has a negative impact on the results of artificial insemination or *in vitro* fertilization (IVF) due to the small size of the eggs [11].

Physiology of obesity: Adults who regulate the amounts of energy (food intake) taken and energy expended are most likely to control or manage their weight, i.e., make it stable for a period of time that may extend to years. This regulation and balance are a result of good communication between the peripheral organs, which include adipose tissue, the digestive system, and the pancreas, with the brain regions. From here, it is known that a positive and sustainable energy balance leads to weight gain and obesity. This mechanism occurs through a complex series of interactions that occur between human biology and external factors (environmental, behavioral, economic). The most significant of these factors is the environment, whether this is external, i.e., what surrounds people, from their lifestyle and the foods they eat, lack of physical activity, lack of sleep, increased stress, or exposure to treatments that cause endocrine disruption; otherwise, it may be internal, i.e., the genetic predisposition of the individual, because not all people are susceptible to weight gain despite being exposed to the same conditions that cause obesity. The gene for obesity is expressed in the central nervous system, and these genes have a capacity that varies from one individual to another, as there are genes that have a large effect on the body mass index (BMI) (a small number) and others that have only a small effect. Heterogeneous mutations that occur in the melanocortin-4 receptor gene are common causes of obesity, especially among children. In addition, infection with various diseases can lead to an increase in adipose tissue [10]. Melanocortin is a system consisting of neural circuits that regulate appetite in humans and animals, and is made up of neurons linked to leptin and ghrelin, which are proteins. This gene controls the production of leptin, a hormone produced by white fat cells that travels to the brain and works to reduce appetite. When a mutation occurs in the gene, this can lead to a significantly reduced production of leptin, thus causing obesity [12].

Materials and Methods: The study included two groups of women: the first group, the control group, consisted of thirty women with weights ranging from 74 - 158 kg and were 30 - 45 years of age; the second group included seventy women who have suffered from infertility for a period of time (3 - 23 years) and whose weights ranged from 90 - 150 kg and the same age groups as the first group. Samples were taken in cooperation with Al-Batoul Teaching Hospital in Mosul, where blood serum (5 ml) was collected and divided into several portions. One such was used to determine the composition and percentage of fatty acids, as shown below. Isolation and extraction of lipids from blood serum Extraction of Blood Lipids [17]،[18] and Using the thin layer chromatography (TLC) technique to separate lipids (CE,TG,PL) [19]

Analysis and Identification of Fatty Acids [20]This study relied on the analysis and re-esterification of fatty acids using boron trifluoride dissolved in methanol at a concentration of 16%. This method was begun by scraping the spot of the fatty compound and placing it in a test tube, adding 2 ml of chloroform, and shaking well. The filtration process was then carried out to remove the silica gel and concentrate the sample to a volume of 1 ml, after which 2 ml of boron trifluoride solution was added to each sample under nitrogen. The solution was then transferred to a closed test tube and placed in a water bath for a period of time that varied according to the type of fatty compound, as shown below:

- Phospholipids: 15 minutes
- Triglycerides: 45 minutes
- Cholesterol ester: 45 minutes

The tubes were then cooled and a mixture of 1 ml pentane + 0.5 ml distilled water was added for the purpose of separating the esterified fatty acids. The separation process was carried out using a centrifuge at a speed of 1006 g for 15 minutes, after which the upper layer of the solution, containing the esters of fatty acids dissolved in the pentane, was separated, then placed in closed tubes for analysis using high-performance liquid chromatography.

Results and Dissection:

Fatty acids level in the phospholipid fraction:

1. Saturated fatty acids (SFAs): This study noted a significant increase in the level of SFAs in this part of the blood serum in infertile women who suffer from being overweight compared to normal women. This may be due to a metabolic disorder in fat metabolism and β-oxidation, which leads to an increase in this type of fatty acid. This is considered an indicator of infertility due to the risk factors posed by these acids, because the increase in these saturated fatty acids greatly affects various metabolic processes, including the process of oxidative phosphorylation in the mitochondria and the association of these acids with polycystic ovary syndrome [21]. Many studies have shown that the increase in the level of fatty acids in the blood serum in both sexes, males and females, leads to an increased likelihood of infertility [22]
2. Unsaturated fatty acids (USFAs): The results of this study showed a significant decrease in the level of monounsaturated fatty acids (MUFAs) and polyunsaturated fatty acids (PUFAs) in this part of the blood serum of infertile women compared to normal women. This may be due to the obesity factor, which greatly affects the functions of the liver and the enzymes released from it, especially those that work in adipose tissue, which negatively affects the metabolism and formation of MUFAs and PUFAs from saturated fatty acids. Thus, this type of fatty acids decreases in the blood serum and affects the occurrence of infertility [23]. Recent studies have shown that a decrease in the level of USFAs in general leads to an increase in the risk of infertility, due to decreased ovulation, by 73% [24].

Table 1
Fatty acids in the phospholipid fraction of blood serum

Fatty Acid	PL		P Value
	Control	HD	
Palmatic	1.4580 ± 0.26582	3.3088 ± 0.15464	<0.01
Stearic	1.3070 ± 0.11016	3.2435 ± 0.04604	<0.01
Sum	2.765 ± 0.37598	6.5523 ± 0.20068	<0.01
Olic	2.5510 ± 0.25124	1.1362 ± 0.05797	<0.01
Lenolic	3.3880 ± 0.19083	1.1500 ± 0.04758	<0.01
Linolenic	1.3120 ± 0.12709	0.2623 ± 0.11417	<0.01
Eicosapentaenoic	0.8470 ± 0.06290	0.2619 ± 0.40198	<0.01
Docosahexaenoic	0.7090 ± 0.07078	0.1450 ± 0.01393	<0.01
Sum	8.807 ± 0.70284	2.9554 ± 0.63563	<0.01

Fatty acids level in the triglyceride fraction:

1. Saturated fatty acids (SFAs): The results of this study showed a significant increase in the level of SFAs in this part of the blood serum in infertile women compared to normal women. The reason for this may be due to the association of the level of this type of fatty acids with that of triglycerides, which is associated with the rate of obesity and the effect on a number of enzymes, especially the hydroxysteroid dehydrogenase enzymes found in the composition of adipose tissue, as its decrease leads to an increase in the level of these fatty acids in the blood serum [25]. In addition, the reason may be the effect of obesity on the occurrence of insulin resistance, which leads to a metabolic disorder in the metabolism and metabolism of triglycerides, which greatly affects this type of fatty acids [26].
2. Unsaturated fatty acids (USFAs): The results of this study showed a significant decrease in the level of MUFAs and PUFAs in this part of the blood serum in infertile women compared to normal women may be due to the nutritional factor that affects triglycerides and the effect of obesity on metabolic disorders in various enzymes, especially elongation and desaturation enzymes. This disorder leads to a lack of conversion and metabolism of saturated fatty acids into MUFAs and PUFAs [27]. A number of studies have also shown a statistical association between the number of eggs and unsaturated fatty acids, especially olic and linolenic. The same studies have also shown a positive association between the number of embryos and the level of olic acid [28].

Table 2
Fatty acids level in the triglyceride fraction of blood serum

Fatty Acid	TG		P Value
	Control	HD	
Palmatic	1.3920 ± 0.20308	3.2708 ± 0.08786	<0.01
Stearic	1.3060 ± 0.22456	3.2465 ± 0.05083	<0.01
Sum	2.6980 ± 0.42764	6.5173 ± 0.13869	<0.01
Olic	2.4370 ± 0.10552	1.1612 ± 0.05218	<0.01
Lenolic	3.3180 ± 0.19234	1.1492 ± 0.03084	<0.01
Linolenic	1.3030 ± 0.05056	0.2888 ± 0.14115	<0.01
Eicosapentaenoic	0.8270 ± 0.08381	0.1881 ± 0.04613	<0.01
Docosahexaenoic	0.7380 ± 0.05959	0.14112 ± 0.01751	<0.01
Sum	8.6230 ± 0.49182	2.92842 ± 0.28781	<0.01

Fatty acid levels in the cholesterol ester fraction

1. Saturated fatty acids (SFAs): The results of this study showed a significant increase in the level of SFAs in this part of the blood serum when comparing infertile women with normal women. This may be due to the high levels of cholesterol in infertile women, which is essential to the formation of cholesterol ester by binding with fatty acids to be transported to different parts of the body. Thus, the level of SFAs associated with this part of the blood serum increases, which is considered a risk factor for infertility in addition to the possibility of early miscarriage due to high cholesterol and the associated SFAs [29]. Studies have shown a negative relationship between high levels of saturated fatty acids and cholesterol and women's fertility due to the effect on a number of hormones related to the fertilization process [30].
2. Unsaturated fatty acids (USFAs): The results of this study showed a significant decrease in the levels of MUFAs and PUFAs in this part of the blood serum in infertile women compared to normal women may be due to several factors, the most important of which is obesity, which greatly affects the formation and metabolism of this type of fatty acids by affecting various enzymes, especially those responsible for removing saturation Δ5 and Δ7, which affect the formation of short-chain USFAs containing 6-12 carbon atoms [31]. A number of studies have found that these short-chain fatty acids

are positively associated with reproductive health and fertility in women through their role in many physiological processes, including immune regulation, and that a deficiency in the levels of these acids is positively associated with the occurrence of complications associated with infertility [30].

Table 3
Fatty acid levels in the cholesterol ester fraction

Fatty Acid	CE		P Value
	Control	HD	
Palmatic	1.4540 ± 0.22377	3.2650 ± 0.11632	<0.01
Stearic	1.3670 ± 0.17544	3.2465 ± 0.04019	<0.01
Sum	2.8210 ± 0.39921	6.5115± 0.15651	<0.01
Olic	2.5190 ± 0.20872	1.1515 ± 0.04037	<0.01
Lenolic	3.3430 ± 0.21577	1.1927 ± 0.21419	<0.01
Linolenic	1.3260 ± 0.11128	0.2819 ± 0.12557	<0.01
Eicosapentaenoic	0.8640 ± 0.05873	0.1969 ± 0.03761	<0.01
Docosahexaenoic	0.7220 ± 0.10326	0.1381± 0.01744	<0.01
Sum	8.7740 ± 0.69776	2.9611 ± 0.43518	<0.01

REFERENCES

[1] T. L. Joon, N. Pillai, C. G. Yap, and N. K. Jahan, "Obesity and Female Infertility—A Review on Mechanisms (Endocrinology)," *OALib*, vol. 09, no. 06, pp. 1–20, 2022, doi: 10.4236/oalib.1108817.

[2] T. Wasilewski, M. Łukaszewicz-Zając, J. Wasilewska, and B. Mroczko, "Biochemistry of infertility," *Clin. Chim. Acta*, vol. 508, pp. 185–190, Sep. 2020, doi: 10.1016/j.cca.2020.05.039.

[3] K. K. Al-hadrawi and R. T. ALGarawy, "The role of some of the level Antioxidant enzymes and Obesity in development infertility women's infertility in Najaf Province Patients, IRAQ," *BIO Web Conf.*, vol. 65, p. 05050, 2023, doi: 10.1051/bioconf/20236505050.

[4] M. Magdum, Md. A. T. Chowdhury, N. Begum, and S. Riya, "Types of Infertility and Its Risk Factors among Infertile Women: A Prospective Study in Dhaka City," *J. Biosci. Med.*, vol. 10, no. 04, pp. 158–168, 2022, doi: 10.4236/jbm.2022.104014.

[5] R. Bala, V. Singh, S. Rajender, and K. Singh, "Environment, Lifestyle, and Female Infertility," *Reprod. Sci.*, vol. 28, no. 3, pp. 617–638, Mar. 2021, doi: 10.1007/s43032-020-00279-3.

[6] G. Lazzarino *et al.*, "Altered Follicular Fluid Metabolic Pattern Correlates with Female Infertility and Outcome Measures of In Vitro Fertilization," *Int. J. Mol. Sci.*, vol. 22, no. 16, p. 8735, Aug. 2021, doi: 10.3390/ijms22168735.

[7] G. Simionescu *et al.*, "The complex relationship between infertility and psychological distress (Review)," *Exp. Ther. Med.*, vol. 21, no. 4, p. 306, Feb. 2021, doi: 10.3892/etm.2021.9737.

[8] I. J. Radhi, N. H. Al-Saadi, and H. H. A. Wahid, "Female Infertility: A Systematic review of the Literature," *Indian J. Public Health Res. Dev.*, vol. 10, no. 5, p. 457, 2019, doi: 10.5958/0976-5506.2019.01045.3.

[9] A. Kumar *et al.*, "Effect of Biochemical Changes on Female Infertility, Especially 'Leptin and Adiponectin' in Eastern Uttar Pradesh," *Int. J. Infertil. Fetal Med.*, vol. 14, no. 2, pp. 80–84, May 2023, doi: 10.5005/jp-journals-10016-1314.

[10] "Female Infertility - Abstract - Europe PMC." Accessed: Dec. 29, 2024. [Online]. Available: https://europepmc.org/article/nbk/nbk556033?ref=staging.enamul.me&client=bot

[11] R. Ahmad and M. Haque, "Obesity: A Doorway to a Molecular Path Leading to Infertility," *Cureus*, vol. 14, no. 10, p. e30770, doi: 10.7759/cureus.30770.

[12] Y. Yang and Y. Xu, "The central melanocortin system and human obesity," *J. Mol. Cell Biol.*, vol. 12, no. 10, pp. 785–797, Oct. 2020, doi: 10.1093/jmcb/mjaa048.

[13] H.-C. Lee-Okada, C. Xue, and T. Yokomizo, "Recent advances on the physiological and pathophysiological roles of polyunsaturated fatty acids and their biosynthetic pathway," *Biochim. Biophys. Acta BBA - Mol. Cell Biol. Lipids*, vol. 1870, no. 1, p. 159564, Jan. 2025, doi: 10.1016/j.bbalip.2024.159564.

[14] B. Kapoor, D. Kapoor, S. Gautam, R. Singh, and S. Bhardwaj, "Dietary Polyunsaturated Fatty Acids (PUFAs): Uses and Potential Health Benefits," *Curr. Nutr. Rep.*, vol. 10, no. 3, pp. 232–242, Jul. 2021, doi: 10.1007/s13668-021-00363-3.

[15] D. J. Machate *et al.*, "Fatty acid diets: regulation of gut microbiota composition and obesity and its related metabolic dysbiosis," *Int. J. Mol. Sci.*, vol. 21, no. 11, p. 4093, 2020.

[16] H. B. Overby and J. F. Ferguson, "Gut microbiota-derived short-chain fatty acids facilitate microbiota: host cross talk and modulate obesity and hypertension," *Curr. Hypertens. Rep.*, vol. 23, pp. 1–10, 2021.
[17] R. K. Saini, P. Prasad, X. Shang, and Y.-S. Keum, "Advances in Lipid Extraction Methods—A Review," *Int. J. Mol. Sci.*, vol. 22, no. 24, p. 13643, Dec. 2021, doi: 10.3390/ijms222413643.
[18] G. Hölzl and P. Dörmann, "Thin-Layer Chromatography," in *Plant Lipids*, vol. 2295, D. Bartels and P. Dörmann, Eds., in Methods in Molecular Biology, vol. 2295. , New York, NY: Springer US, 2021, pp. 29–41. doi: 10.1007/978-1-0716-1362-7_3.
[19] M. Wang, Y. Zhang, R. Wang, Z. Wang, B. Yang, and H. Kuang, "An Evolving Technology That Integrates Classical Methods with Continuous Technological Developments: Thin-Layer Chromatography Bioautography," *Molecules*, vol. 26, no. 15, p. 4647, Jul. 2021, doi: 10.3390/molecules26154647.
[20] N. Al-Rashidee, M. Al-Sharok, and M. Al-Obaidi, "Spectrophotometric Determination of some Pharmacological Compounds Used in The Treatment of Heart Attacks and Follow-Up of Biochemical Changes," Thesis, Mosul, Iraq, 2023.
[21] H. Kobayashi and S. Imanaka, "Recent progress in metabolomics for analyzing common infertility conditions that affect ovarian function," *Reprod. Med. Biol.*, vol. 23, no. 1, p. e12609, Jan. 2024, doi: 10.1002/rmb2.12609.
[22] K. R. Dunning, D. L. Russell, and R. L. Robker, "Lipids and oocyte developmental competence: The role of fatty acids and β-oxidation," *Reproduction*, vol. 148, no. 1, pp. R15–R27, Jul. 2014, doi: 10.1530/REP-13-0251.
[23] H. Çekici and Y. Akdevelioğlu, "The association between trans fatty acids, infertility and fetal life: a review," *Hum. Fertil.*, vol. 22, no. 3, pp. 154–163, Jul. 2019, doi: 10.1080/14647273.2018.1432078.
[24] "Correlation of Erythrocyte Trans Fatty Acids with Ovulatory Disorder Infertility in Polycystic Ovarian Syndrome," *Adv. Biosci. Clin. Med.*, vol. 2, no. 2, Jul. 2014, doi: 10.7575/aiac.abcmed.14.02.02.04.
[25] J. C. Lopez-Alvarenga, S. O. E. Ebbesson, L. O. E. Ebbesson, M. E. Tejero, V. S. Voruganti, and A. G. Comuzzie, "Polyunsaturated fatty acids effect on serum triglycerides concentration in the presence of metabolic syndrome components. The Alaska-Siberia Project," *Metabolism*, vol. 59, no. 1, pp. 86–92, Jan. 2010, doi: 10.1016/j.metabol.2009.07.010.
[26] S. A. Dawood, H. A. L. Mossa, and M. A. Jwad, "Influence of Obesity and Insulin Resistance on the Reproductive Outcome of Iraqi Women Undergoing Intracytoplasmic Sperm Injection," *Al-Rafidain J. Med. Sci. ISSN 2789-3219*, vol. 6, no. 1, pp. 179–187, Feb. 2024, doi: 10.54133/ajms.v6i1.580.
[27] A. Czumaj *et al.*, "Alterations of Fatty Acid Profile May Contribute to Dyslipidemia in Chronic Kidney Disease by Influencing Hepatocyte Metabolism," *Int. J. Mol. Sci.*, vol. 20, no. 10, p. 2470, May 2019, doi: 10.3390/ijms20102470.
[28] R. Zarezadeh, M. Nouri, K. Hamdi, M. Shaaker, A. Mehdizadeh, and M. Darabi, "Fatty acids of follicular fluid phospholipids and triglycerides display distinct association with IVF outcomes," *Reprod. Biomed. Online*, vol. 42, no. 2, pp. 301–309, Feb. 2021, doi: 10.1016/j.rbmo.2020.09.024.
[29] J. Castillo *et al.*, "Proteomic Changes in Human Sperm During Sequential in vitro Capacitation and Acrosome Reaction," *Front. Cell Dev. Biol.*, vol. 7, Nov. 2019, doi: 10.3389/fcell.2019.00295.
[30] A. Acharya, S. S. Shetty, and S. Kumari N, "Role of gut microbiota derived short chain fatty acid metabolites in modulating female reproductive health," *Hum. Nutr. Metab.*, vol. 36, p. 200256, Jun. 2024, doi: 10.1016/j.hnm.2024.200256.
[31] P. G. Roopashree, S. S. Shetty, and N. Suchetha Kumari, "Effect of medium chain fatty acid in human health and disease," *J. Funct. Foods*, vol. 87, p. 104724, Dec. 2021, doi: 10.1016/j.jff.2021.104724.